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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/826,113	04/16/2004	Piotr Chomczynski	CNA / 19	1054

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EXAMINER	
BABIC, CHRISTOPHER M	
ART UNIT	PAPER NUMBER
1637	

MAIL DATE	DELIVERY MODE
03/18/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/826,113	CHOMCZYNSKI, PIOTR	
	Examiner	Art Unit	
	CHRISTOPHER M. BABIC	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29-31,41,44,46-52 and 59-63* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *44, 62, and 63* is/are allowed.

6)☒ Claim(s) *29-39,41,46-52 and 59-61* is/are rejected.

7)☒ Claim(s) *31* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 18, 2007 has been entered. Claim(s) 29-31, 41, 44, 46-52, and 59-63 are pending.

Examiner of Record

As an initial matter, it is noted that the Examiner of record has been changed from Jeffery Fredman, Art Unit 1637, to Christopher M. Babic, Art Unit 1637.

New Grounds Claim Objections

Claim(s) 31 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Step (a) of claim 29 already requires at least one ribonuclease inhibitor.

New Grounds Claim Rejections - 35 USC § 112 - Indefiniteness

The following new grounds of rejection is made in view of a newly discovered indefiniteness within the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim(s) 50 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 50 recites the limitation "the hydrophobic organic solvent" in line 1. There is insufficient antecedent basis for this limitation in claim 47.

Claim Rejections - 35 USC § 112 - Scope of Enablement - Withdrawn

Applicant's remarks (pg. 12-13) regarding the rejection of claim(s) 29-39, 41, 46-52, and 59-61 are sufficient to overcome the grounds of the rejection. Thus, the rejection has been withdrawn.

Claim Rejections - 35 USC § 102 - Withdrawn

Applicant's remarks (bottom pg. 8) regarding the rejection of claim(s) 29-39, 41, 46-52, and 59-61 over Chen are sufficient to overcome the grounds of the rejection. Chen does not teach maintaining pH in the range from about 3.6 to below 4.0. Thus, the rejection has been withdrawn.

Maintained Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim(s) 29-39, 41, 46-52, and 59-61 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al. (Chinese patent 1,220,995, translation provided) in view of Chomczynski (U.S. 5,346,994).

Chen teaches a method for isolating purified RNA from a biological sample of claims 29 and 59 (see page 3, bottom half, for example or page 4) comprising: a) treating the sample comprising phenol at a final concentration ranging from about 10% w/w to about 60% w/w and at least one ribonuclease inhibitor (see page 6, where 12-46% phenol is used in conjunction with guanidine isothiocyanate, an RNAse inhibitor and see page 8, preferred embodiment 2, step 1, where the phenol reagent with 30% w/w is added to the tissue), b) mixing the sample with at least one hydrophobic solvent and a buffer at a concentration sufficient to maintain a pH in the range from about pH 3.6 to below pH 4.0 (see page 8, preferred embodiment 2, where the pH of the phenol reagent is pH 3.5, which is about 3.6 and where the hydrophobic solvent chl0roform/isoamyl alcohol

is added to the solution. Further note that Chen teaches overlapping ranges of pH from 3.5 to 6.5 and the use of glacial acetic acid to regulate the pH value (see page 3)), c) recovering the purified RNA from an aqueous phase to which about an equal volume of a water soluble organic solvent is added to precipitate the purified RNA (See page 8, preferred embodiment 2, where the aqueous phase is precipitated with isopropanol), d) washing and solubilizing the precipitated RNA (see page 9, where the RNA precipitate is washed with alcohol and dissolved in a buffer).

With regard to claim 30, Chen teaches the use of acetate and citrate buffers (see page 8, preferred embodiment 2, lines 3 and 4).

With regard to claims 31-34, Chen teaches the use of ribonuclease inhibitors (see page 8, preferred embodiment 2, line 1, where the chaotropic salt guanidine isothiocyanate is used as an RNAse inhibitor at a concentration in the range of 0.5 M to about 6M).

With regard to claims 35-36, Chen teaches the use of detergents such as SDS and sarcosine including a range of 0.1.% SDS (see page 8, preferred embodiment 2, lines 2-3).

With regard to claims 37-39, Chen teaches the use of sodium acetate and trisodium citrate, where claim 38 indicates that acetate is a preferred salt and claim 39 indicates that citrate is a preferred chelating agent).

With regard to claim 41, Chen teachesthe use of Guanidine salts (see page 8, line 1).

With regard to claims 46, Chen teaches a pH range of 3.5-6.5 and exemplifies a pH of 3.5 (see page 3 and see page 8, preferred embodiment 2).

With regard to claims 46, Chen teaches a pH range of 3.5-6.5 and exemplifies a pH of 3.5 (see page 3 and see page 8, preferred embodiment 2).

With regard to claims 47-49, Chen teaches the steps of: a) treatment with the monophase reagent comprising phenol in concentrations from 12-46% w/w (see page 6) with a pH from 3.5-6.5 (see page 3) and a chaotrope (see page 6 where guanidine isothiocyanate is used); b) sedimenting the sample to obtain a purified sample substantially free of DNA, proteins and cellular components(see page 8, where the step of centrifugation is a form of sedimentation that will remove DNA, proteins and cellular components); c) adding to the purified sample about an equal volume of a water soluble organic solvent to precipitate the purified RNA (See page 8, preferred embodiment 2, where the aqueous phase is precipitated with isopropanol); d) sedimenting the precipitated RNA (see page 8, last sentence); e) washing and solubilizing the precipitated RNA (see page 9, first five sentences).

With regard to claim 50, Chen teaches the use of chloroform (see page 8, middle of the page).

With regard to claim 51, Chen teaches addition of a composition which can be at "about 1.5 X" concentration (see page 8).

With regard to claim 52, 60, 61, Chen teaches precipitation with isopropanol (see page 8).

While Chen teaches the use of a pH adjusting component, Chen does not state that the amount used will be sufficient to maintain pH.

Chomczynski teaches the use of a pH adjusting component in an RNA solvent solution where "the solvent solution may include a buffering component, such as sodium acetate or sodium citrate, in an amount sufficient to maintain the pH of the solution (see column 3, lines 17-22)."

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the isolation buffer of Chen, who notes a desire to "regulate the pH value (see page 3)", to incorporate enough buffering component as taught by Chomczynski since Chomczynski •notes "the solvent solution may include a buffering component, such as sodium acetate or sodium citrate, in an amount sufficient to maintain the pH of the solution (see column 3, lines 17-22)." An ordinary practitioner would have been motivated to include sufficient buffering in the isolation buffer of Chen in order to maintain the pH since both Chen and Chomczynski teach and motivate the use of buffering components to maintain the pH of the solution.

Response to Arguments

Applicant's arguments have been fully considered but they are not persuasive.

As understood by the examiner, Applicant first argues that, in contrast to the present invention, the methods of Chen do not produce RNA free from contaminating DNA, and more specifically, that Chen does not indicate that the

claimed pH range is beneficial for the effective removal of DNA. This argument is not persuasive because Chomczynski provides the requisite motivation to maintain the buffer solution of Chen at "about" 3.6 to below 4. The fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

It appears from the last Office communication dated September 18, 2007, that Applicant has attempted to rebut this obviousness rejection by asserting that the claimed invention produces unexpected results relative to the combination of Chen and Chomczynski (see declaration filed January 17, 2007). The current examiner of record has reviewed the 1/17/2008 declaration and agrees with the previous examiner that the declaration provides proof of unexpected results relative to Chen regarding the presence of DNA with respect to **particular** embodiments of a pH of 3.8, 40% phenol, 4M guanidine, 5% glycerol, 0.1% sarcosine, and 10mM sodium citrate. This example does not provide support that other conditions, such as pH 3.5, which must literally be within the scope of "about pH 3.6", if anything is, or other reagent conditions, will achieve the same results. Furthermore, one of Applicant's main arguments as to the reason for the unexpected results is that a "scaling agent" as in Chen's method, is not present in the concentration Chen uses. This is not a requirement of the claimed inventions. Thus, the claimed inventions are not commensurate in scope with the declaration. As MPEP 716.02(d) notes "the "objective evidence of

nonobviousness must be commensurate in scope with the claims which the evidence is offered to support."

With regard to Applicant's remarks highlighting the differences between the claimed methods, these arguments are not persuasive because every limitation within each method is taught and/or suggested by the combination of references.

Thus, the rejection is maintained.

Allowable Subject Matter

Claims 44, 62, and 63 are allowable for the reasons set forth in the Office Action dated September 18, 2007.

Conclusion

Claim(s) 31 is objected to.

Claim(s) 29-39, 41, 46-52, and 59-61 are rejected.

Claim(s) 44, 62, and 63 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher M. Babic whose telephone number is 571-272-8507. The examiner can normally be reached on Monday-Friday 7:00AM to 4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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